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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/785,793	02/16/2001	Bertrand Seraphin	70436	5538

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/785,793	Applicant(s) SERAPHIN ET AL.	
	Examiner Ja-Na Hines	Art Unit 1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 07 February 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1-12*.
   Claim(s) withdrawn from consideration: *None*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See continuation page.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

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The scope of enablement rejection of claims 1-12 under 35 U.S.C. 112, first paragraph, is maintained for reasons already of record. Applicants argue that one of skill would know how to provide an expresion environment. However the issue is not providing an expression environment, the issue is that the claims are not enabled for a method for detecting and/or purifying biomolecules and/or protein complexes, the method comprising: (a) providing an expression environment containing one or more heterologous nucleic acids encoding one or more subunits of a biomolecule complex; (b) maintaining the expression environment under conditions that facilitate expression of the one or more subunits in a native form as fusion proteins with subunits being fused to at least two different affinity tags, wherein one of the affinity tags consists of one or more IgG binding domains of Staphylococcus protein A; (c) purifying the one or more subunits by a combinations of at least two different affinity purification steps each comprising binding the one or more subunits via one affinity tag to a support material capable of selectively binding one of the affinity tags and separating the one or more subunits from the support material after substances not bound to the support material have been removed to provide a purified biomolecule and/or protein complex; and (d) detecting the purified biomolecule and/or protein complex. And applicants effort to point to references concerning expression environments and vectors, does not overcome the enablement issue.

Moreover, the claim language drawn to heterologous nucleic acids encoding one or more subunits of a biomolecule complex embraces sequences without disclosing the actual nucleic acid sequences. Applicants urge that a skilled person could easily identify a corresponding nucleic acid. However, the claims are not enabled to embrace limitless heterologous nucleic acids. It is noted that the claims comprise one or more heterologous nucleic acids without any limit, therefore without specific information regarding the heterologous nucleic acids, one of skill in the art could not predict which heterologous nucleic acids would result in the desired encoded one or more subunits of a biomolecule complex, thereby requiring undue experimentation. Therefore, despite applicants' assertion to the contrary, one of skill in the art would be required to perform undue experimentation to use the claimed method for detecting and/or purifying biomolecules and/or protein complexes.

Applicants' assert that only routine experimentation is required. However, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims, contrary to applicants' arguments. The instant examples recite that a method comprises providing a vector encoding a fusion of a yeast protein to the Calmodulin Binding Peptide-Tobacco Etch Virus protease NIA –Staphylococcus Protein A (CBP-TEV-Protein A) double tag wherein the fusion protein is one subunit of a protein complex of yeast containing 24 subunits and the plasmid is transformed in to the yeast cell. There are no examples commensurate in scope to the broad claims. The claims are only enabled for complexes from a yeast host. The claims are only enabled for encoding a fusion of a yeast protein to the Calmodulin Binding Peptide-Tobacco Etch Virus protease NIA –Staphylococcus Protein A (CBP-TEV-Protein A) double tag wherein the fusion protein is one subunit of a protein complex of yeast containing 24 subunits and the plasmid is transformed in to the yeast cell. The claims are not enabled for providing a generic expression environment containing any type of heterologous nucleic acids encoding one or more subunits of a biomolecule complex, since this includes unidentified heterologous nucleic acids. Also, the claims are only enabled when the method also comprises concentrating the eluted proteins using precipitation techniques; and detecting the concentrated proteins by polyacrylamide gel electrophoreses. And applicants document references fail to overcome the rejection.

The teaching within the specification is limited to the specific steps and reagents recited in the instant specification. The specification fails to teach examples of detection and purify biomoleucles and protein complexes, such that without the exact and precise method steps and specific reagents the claimed detection and purification methods could not be achieved. The broad method claims do not require the precise and active steps and reagents thus, one of ordinary skill in the art would be required to determine the appropriate reagents and conditions required to achieve the claimed method. Therefore, applicants assertions that the references would enable one skilled in the art to make and use the claimed invention are irrelevent, since the cited references refer to exact and precise method steps and specific reagent. Therefore, the guidance presented is narrowly tailored to the working examples and not to the broad claims. The prior art states that only yeast cells were enabled at the time of applicants' invention. Thus, applicants' assertions are not persuasive.

Applicants' broadly state that each individual aspect of the claims would have been routine to one skilled in the art, however it is the examiner's position that without the exact and precise method steps and specific reagents the claimed detection and purification methods could not be achieved. Moreover, applicants' own disclosure and articles presented supports that without exact and precise method steps and specific reagents the claimed detection and purification methods could not be achieved.

Therefore, one skilled in the art could not make and/or use the invention without undue experimentation and the rejection is maintained. Applicants generalization that no undue experimentation is required is not found persuasive in view of the quantity of experimentation, lack of guidance and working examples and the state of the prior art. Therefore the rejection is maintained and applicants arguments are not persaussive.

The written description rejection of claims 1-12 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons already of record. The rejection was on the grounds that the specification and claims lack sufficient written description of the generically claimed an expression environment containing one or more heterologous nucleic acids encoding one or more subunits of a biomolecule complex.

Applicants' urge that the one of ordinary skill in the art would clearly understand how to provide an expression environment containing one or more heterologous nucleic acids encoding one or more subunits of a biomolecule complex. However, it is noted that the one or more heterologous nucleic acids are defined by their activity or function, i.e., the ability to encode one or more subunits of a biomolecule complex and does not describe the one or more heterologous nucleic acids. As previously stated, the encoding distinction is a purely functional distinction and a description of the heterologous nucleic acid by what it does, such as encoding one or more subunits of a biomolecule complex is insufficient. The written description of the one or more heterologous nucleic acids encoding one or more subunits of a biomolecule complex is insufficient when the specification fails to disclose an example of heterologous nucleic acid sequences that can be used in the claimed method. Moreover, applicants' article references do not overcome the rejection.

The specification does not provide evidence that a single heterologous nucleic acid, as claimed, functions with the ability to encoded one or more subunits of a biomolecule complex. And applicants have not provided evidence to the contrary. The instant specification and claims are encompassing currently unknown sequences and claims that these nucleic acid sequences can be used to in the method of detection and purification. Therefore is evident that other heterologous nucleic acids have not yet been identified. Moreover, the instant specification fails to disclose specific heterologous nucleic acid sequences; rather the specification broadly defines the sequences to be any and every nucleic acid sequence without any discretion. In view of the lack of evidence, it is apparent that Applicants were not

in possession of all or many heterologous nucleic acid sequences that encode one or more subunits of a biomolecule complex at the time of filing the instant application. The skilled artisan cannot envision the detailed structure of a method for detecting and/or purifying biomolecule and/or protein complexes in the method comprising providing an expression environment containing one or more heterologous nucleic acids encoding one or more subunits of a biomolecules complex. Thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation despite applicants' assertions to the contrary.

Thus, the one or more heterologous nucleic acids described only by their ability to encode fails to meet the written description requirements. Therefore the rejection is maintained since applicants' arguments and assertions are not persaussive.

The rejection of claims 1-12 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained. The preamble of the claims is drawn to a method for detecting and/or purifying biomolecules and/or protein complexes, and recites purification and detection in the alternative. However the amended steps recite and require both a purification step and a detection step. Therefore, the body of the claims recites both steps even though the preamble recites alternative language. Thus, appropriate claim language is required to make the preamble and the body of the claim commensurate in scope.